- **CLAIMS**

1. A polypeptide possessing a phosphodiesterase catalytic activity at least about 6 fold, preferably about 8 or 10 fold, most preferably 15 to 20 fold higher than the phosphodiesterase catalytic activity of an endogenous full length PDE7 protein which comprises at least the catalytic domain of the PDE7 with the exception of the amino acid sequence disclosed by Michaeli et al (1993, J. Biol. Chem., 268, 12925-12932) as the sequence consisting of the NH2 terminal deletion of HCP1 generated by sequential deletion of the sequence from the first ATG codon to residue 81 (L22M2).

2. A polypeptide according to claim 1 of up to about 427 amino acids in length possessing a phosphodiesterase 7 catalytic domain and comprising at least 312 consecutive amino acids of a sequence selected from the group consisting of the amino acid sequences of SEQ ID N° 1, 2 or 3; or a homologous polypeptide thereof.

3. The polypeptide according to claim 2 which comprises the aminoacid sequence which:

- begins at the aminoacid residue located in position 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 ,11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64 of SEQ ID N°1, 2 or 3; and which

- ends at the aminoacid residue located in position 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 934, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404,

405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427 of SEQ ID N°1, 2 or 3 or a homologous peptide thereof.

4. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 5 and ending at the amino acid residue in position 427 of SEQ ID N°1, 2 or 3; or a homologous polypeptide thereof.

5. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 25 and ending at the amino acid residue in position 427 of SEQ ID N°1, 2 or 3; or a homologous polypeptide thereof.

6. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 45 and ending at the amino acid residue in position 427 of SEQ ID N°1, 2 or 3; or a homologous polypeptide thereof.

7. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 5 and ending at the amino acid residue in position 394 of SEQ ID N°1, 2 or 3; or a homologous polypeptide thereof.

8. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 25 and ending at the amino acid residue in position 394 of SEQ ID N°1, 2 or 3; or a homologous polypeptide thereof.

9. The polypeptide according to claim 3 which comprises the amino acid sequence beginning at the amino acid residue in position 45 and ending

at the amino acid residue in position 394 of SEQ ID N° 1, 2 or 3; or a homologous polypeptide thereof.

10. A polypeptide having at least 80% homology or identity, preferably 85% homology or identity, with a polypeptide as defined in anyone of claims 1 to 9.

11. A polypeptide having at least 90% homology or identity, preferably 95% homology or identity, most preferably 99 % homology or identity with a polypeptide as defined in anyone of claims 1 to 9.

12. A polypeptide comprising the amino acid sequence which begins at an amino acid comprised between amino acids 57 to 100 and ends at an amino acid comprised between amino acids 450 to 483 of the full-length PDE7(A) protein with the exception of the amino acid sequence disclosed by Michaeli et al (1993, J. Biol. Chem., 268, 12925-12932) as the sequence consisting of the NH2 terminal deletion of HCP1 generated by sequential deletion of the sequence from the first ATG codon to residue 81 (L22M2).

13. A polypeptide according to claim 12 wherein the PDE7A protein is human PDE7A1 or PDE7A2.

14. A nucleic acid sequence encoding a polypeptide as defined in anyone of claims 1 to 13, or a sequence complementary thereto.

15. The nucleic acid sequence according to claim 14 which is selected from the group consisting of the nucleic acid sequences of SEQ ID N°4, 5 or 6; or a sequence complementary thereto.

16. A nucleic acid sequence comprising the portion of the sequence of the full length PDE7(A) which remains after deletion of a nucleic acid sequence according to claims 14 to 15.

17. A nucleic acid sequence according to anyone of claims 14 to 16 which is of genomic origins.

18. A nucleic acid sequence according to claim 16 or 17 wherein the deleted nucleic acid portion is replaced by a heterologous polynucleotide sequence.

19. A polypeptide according to anyone of claim 1 to 13 or a nucleic acid d sequence according to anyone of claims 14 to 18, wherein PDE7(A) is of human, mouse or rat origin, most preferably human .

20. The nucleic acid according to claim 18, wherein the heterologous polynucleotide comprises a selection marker.

21. The nucleic acid according to claim 18, wherein the heterologous polynucleotide comprises at least a *lox*P sequence at its 5' end and at least a *lox*P sequence at its 3' end.

22. The nucleic acid of any one of anyone of claims 14 to 21, wherein the nucleic acid sequence encoding a polypeptide according to claim 2 is operably linked to a regulatory sequence.

23. A nucleic acid according to claim 22, wherein the regulatory sequence consists of an inducible promoter.

24. The nucleic acid sequence according to claim 23, wherein the regulatory sequence consists of a promoter inducible by an inducer such as Ponasterone.

25. A recombinant vector comprising a nucleic acid sequence as defined in claims 14 to 24.

26. A recombinant host cell comprising a nucleic acid as defined in claims 14 to 24.

27. A recombinant host cell comprising a recombinant vector according to claim 25.

28 A recombinant host cell according to claims 26 or 27 which is eukaryotic.

29. The recombinant host cell according to anyone of claims 26 to 28 which is selected from the group of recombinant hosts cell consisting of zygotes, embryonic, foetal or adult pluripotent stem cells, recombinant hosts cell derived from mammal blastomeres or blastocysts and ES cells.

30. A knock out animal generated by the use of a vector comprising a polynucleotide construct with a sequence comprising the portion of the full length PDE7 which remains after deletion of a nucleic acid according to anyone of claims 14 to 24, said construct replacing thus a portion of the naturally occuring PDE7 sequence within the genome of this animal.

31. A knock out animal according to claim 30 of mammalian origin.

32. A knock out animal according to claim 31 of murine or rat origin.

33. A method for producing a polypeptide as defined in claims 1 to 13, wherein said method comprises the steps of:

a) culturing, in an appropriate culture medium, a recombinant host cell as defined in claims 26 to 29;

b) harvesting the medium thus conditioned or lyse the recombinant host cell;

c) separating or purifying, from the said culture medium, or from the resultant cell lysate, the thus produced polypeptide.

34. A method for the *in vitro* screening of a compound that inhibits PDE7 phosphodiesterase activity, wherein said method comprises the steps of:

a) providing a desired amount of a polypeptide as defined in claims 1 to 13;

b) adding the desired amount of a polypeptide provided in step a) to a buffer solution containing a desired amount of a candidate compound to be assayed;

c) measuring the phosphodiesterase enzyme activity ; and

d) comparing the measured enzyme activity obtained at step c) with the enzyme activity obtained in the absence of the candidate compound.

35. A method according to claim 34 wherein the polypeptide provided at step a) consists of the amino acid sequence beginning at the amino acid residue in position 45 and ending at the amino acid residue in position 427 of SEQ ID N° 1, or a homologous polypeptide thereof.

36. A method according to claims 34 or 35 wherein the polypeptide originates from the cell lysate of a host cell transfected with a nucleic acid as defined in claims 14 to 24 or with a recombinant vector according to claim 25.

37. A method according to claim 34 or 36, wherein the phosphodiesterase catalytic activity is measured as the level of hydrolysis of cAMP.

38. A method for the *in vitro* screening of a compound that inhibits PDE7 phosphodiesterase activity, wherein said method comprises the steps of:

a) Cultivating a recombinant host cell as defined in claims 26 to 29 in an appropriate culture medium;

b) adding a desired concentration of the candidate compound to be assayed in said culture medium;

c) measuring the intracellular phosphodiesterase enzyme activity ; and

d) comparing the enzyme activity obtained at step c) with the enzyme activity obtained when step b) is omitted.

39. The method according to claim 38, wherein the recombinant host cell consists of a CHO cell line expressing the dimeric ecdysone receptor.

40. The method according to claim 38, wherein the recombinant host cell has been transfected with a recombinant vector comprising a nucleic acid encoding a polypeptide as defined in claims 1 to 13 which is operably linked to an inducible regulatory sequence.

41. The method according to claim 40, wherein the regulatory sequence is inducible by an inducer.

42. The method according to claim 41, wherein the inducer is Ponasterone.

43. The method according to anyone of claims 38 to 42, wherein before step b), the recombinant hosts cell are cultivated in the presence of the inducer which activates the inducible regulatory sequence during step a).

44. The method according to anyone of claims 38 to 43,, wherein an adenylate cyclase activator is added at the end of step b), before the addition of a stop solution.

45. The method according to anyone of claims 38 to 44,, wherein the phosphodiesterase enzyme activity is measured after cell lysis through the measure of the amount of intracellular cAMP produced during step b).

46. A method for the *in vitro* screening of a compound that inhibits PDE7 activity, wherein said method comprises the steps of:

a) providing a recombinant host cell coexpressing a polypeptide according to anyone of claims 1 to 13 and a reporter gene, in an appropriate culture medium;

b) adding a desired concentration of the candidate compound to be assayed in said culture medium;

c) measuring the reporter gene expression; and

d) comparing the enzyme activity obtained at step c) with the enzyme activity obtained when step b) is omitted.

47. The method according to claim 46, wherein the recombinant host cell consists of a CHO cell line expressing the dimeric ecdysone receptor.

48. The method according to claims 46 or 47, wherein the recombinant host cell has been transfected with a recombinant vector comprising a nucleic acid encoding a polypeptide as defined in claims 1 to 13 which is operably linked to an inducible regulatory sequence.

49. The method according to claim 48, wherein the regulatory sequence is inducible by an inducer such as Ponasterone.

50. The method according to anyone of claims 46 to 49, wherein before step b), the recombinant hosts cell are cultivated in the presence of the inducer which activates the inducible regulatory sequence during step a).

51. The method according to anyone of claims 46 to 50, wherein an adenylate cyclase activator is added at the end of step b), before the addition of a stop solution.

52. the method of claims 46 to 51 wherein the reporter gene is a beta lactamase gene.

53. A kit for the *in vitro* screening of a compound that inhibits PDE7 phosphodiesterase catalytic activity, wherein said kit comprises:

a) a polypeptide as defined in claims 1 to 13;

b) optionally, the reagents necessary to perform the phosphodiesterase catalytic activity measures.

54. A kit for the *in vitro* screening of a compound that inhibits PDE7 phosphodiesterase catalytic activity, wherein said kit comprises:

a) a recombinant host cell as defined in claims 26 to 29;

b) optionally, the reagents necessary to perform the phosphodiesterase catalytic activity measurement.

55. A kit for the in vitro screening of a compound that inhibits PDE7 phosphodiesterase activity, wherein said kit comprises :

a) a recombinant host cell of the invention coexpressing a polypeptide as defined in claims 1 to 13 and a reporter gene; and

b) optionally, the reagents necessary to perform the reporter gene expression measurement.

56. A method for selecting in vitro a compound that inhibits PDE7 phosphodiesterase activity, wherein said method comprises the steps of:
a) performing the method as defined in claims 34 to 37 with a candidate compound; and in case that said candidate compound is found to inhibit the phosphodiesterase activity, then
b) performing the method as defined in claims 38 to 52 with the inhibitor compound selected at step a)

57. A method for selecting a compound that selectively inhibits PDE7 phosphodiesterase activity, wherein said method comprises the steps of:
a) selecting a compound which inhibits PDE7 phosphodiesterase activity by carrying out a method as defined in claims 34 to 37, 38 to 52 and 56; and
b) assaying the selected inhibitor compound for its inability to inhibit the phosphodiesterase activity of at least one PDE enzyme other than PDE7.

58. The method according to claim 57, wherein the selected inhibitor is assayed for its inability to inhibit the phosphodiesterase activity of PDE3 and PDE4 enzymes.

59. The method according to claim 57, wherein the selected inhibitor is assayed for its inability to inhibit the phosphodiesterase activity of PDE1, PDE2, PDE3, PDE4, PDE5 and PDE6 enzymes.

60. A phosphodiesterase inhibitor compound selected according to a method as defined in claims 34 to 37, 38 to 52, 56 and 57 to 59.

61. The use of a phosphodiesterase inhibitor compound selected according to a method as defined in claims 34 to 37, 38 to 52, 56 and 57 to 59.
for manufacturing a pharmaceutical composition.

62. The use of a compound obtainable identifiable, selectable, or characterizable by the method according to anyone of claims 34 to 52 and 56 to 59 for the manufacture of a pharmaceutical composition to be used in the treatment, diagnosis or surgery of the human or animal.

64. The use of a compound obtained, identified, selected or characterized by the method according to anyone of claims 34 to 52 and 56 to 59 for the manufacture of a pharmaceutical composition to be used in the treatment, diagnosis or surgery of the human or animal.

65. The use of a compound obtained, identified, selected or characterized by the method according to anyone of claims 34 to 52 and 56 to 59 for the manufacture of a pharmaceutical composition for the treatment or prevention of various pathological conditions such as diseases affecting the immune system, including AIDS, rejection of transplant, auto-immune disorders such as T-cells related diseases for example rheumatoid arthritis; inflammatory diseases such as respiratory inflammation diseases including chronic obstructive pulmonary disease (COPD), asthma; gastrointestinal inflammation diseases such as Crohn's disease, colitis, pancreatitis as well as different types of cancers including leukaemia.

66. The use of a compound obtainable, identifiable, selectable or characterizable by the method according to anyone of claims 34 to 52 and 56 to 59 for the manufacture of a pharmaceutical composition for the treatment or prevention of various pathological conditions such as

diseases affecting the immune system, including AIDS, rejection of transplant, auto-immune disorders such as T-cells related diseases for example rheumatoid arthritis; inflammatory diseases such as respiratory inflammation diseases including chronic obstructive pulmonary disease (COPD), asthma; gastrointestinal inflammation diseases such as Crohn's disease, colitis, pancreatitis as well as different types of cancers including leukaemia

67. The use of a compound obtained, identified, selected or characterized by the method according to anyone of claims 34 to 52 and 56 to 59 in the synthesis of a compound for the treatment or prevention of various pathological conditions such as diseases affecting the immune system, including AIDS, rejection of transplant, auto-immune disorders such as T-cells related diseases for example rheumatoid arthritis; inflammatory diseases such as respiratory inflammation diseases including chronic obstructive pulmonary disease (COPD), asthma; gastrointestinal inflammation diseases such as Crohn's disease, colitis, pancreatitis as well as different types of cancers including leukaemia